



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<b>(21) International Application Number:</b> PCT/AU98/00805 <b>(22) International Filing Date:</b> 24 September 1998 (24.09.98) <b>(30) Priority Data:</b> PO 9386 24 September 1997 (24.09.97) AU <b>(71) Applicant (for all designated States except US):</b> GARVAN INSTITUTE OF MEDICAL RESEARCH [AU/AU]; c/o St. Vincent's Hospital, 384 Victoria Street, Darlinghurst, NSW 2010 (AU). <b>(72) Inventor; and</b> <b>(75) Inventor/Applicant (for US only):</b> HERZOG, Herbert [AT/AU]; 17-318 Bondi Road, Bondi, NSW 2026 (AU). <b>(74) Agent:</b> F.B. RICE & CO.; 605 Darling Street, Balmain, NSW 2041 (AU).		<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> NOVEL RECEPTOR  <b>(57) Abstract</b>  The invention provides isolated polynucleotide molecules encoding a novel G-protein-coupled receptor (designated TSR32). These isolated polynucleotide molecules can be used to express the receptor in cells which can then be used to screen compounds for agonist and antagonist activity.		

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## NOVEL RECEPTOR

### Field of the Invention:-

The present invention relates to isolated polynucleotide molecules which encode a novel seven-transmembrane G-protein-coupled receptor designated TSR32. In addition, the present invention relates to the use of these molecules in the production of TSR32 receptors using recombinant technology and to methods of screening compounds for agonists and/or antagonists of the TSR32 receptor.

### Background of the Invention:-

Proteins with seven-transmembrane (7TM) segments define a superfamily of receptors with a common structure comprising an extracellular N-terminus, three extramembranous loops on either side of the plasma membrane, and a cytoplasmic C-terminus. The majority of such proteins function as cell-surface receptors for a variety of ligands, including small molecules, peptides, hormones, ions, and external sensory stimuli such as odorants (Watson, S. and Arkininstall, S., The G-protein Linked Receptor Facts Book, Academic Press, London, 1994). One family within the 7TM superfamily is known as the secretin receptor family and comprises member receptors with specificity for secretin, calcitonin, glucagon, glucagon-like peptide 1, parathyroid hormone, parathyroid-related peptide, corticotropin-releasing factor (CRF), growth hormone-releasing hormone (GHRH), gastric inhibitory polypeptide, pituitary adenylate-cyclase-activating polypeptide (PACAP), vasoactive intestinal peptides (VIP) and insect diuretic hormone (DHR).

The present inventor has now identified a further member receptor of the secretin receptor family. This receptor, designated TSR32, appears to be expressed in a large variety of tissue types including heart, kidney, lung and brain with highest levels in the thyroid gland. Since agonists and/or antagonists for this receptor may have commercial value, for example as regulators of important thyroid functions in growth, development and metabolic activity, the ability to produce TSR32 receptors by recombinant DNA technology would be advantageous.

**Disclosure of the Invention:-**

Thus, in a first aspect, the present invention provides an isolated polynucleotide molecule encoding a G-protein-coupled receptor, designated TSR32, which is characterised by the N-terminal amino acid sequence:

5 MTPQSLQTT (SEQ ID NO: 1),  
or a functionally equivalent fragment of said receptor.

Preferably, the polynucleotide molecule encodes a human TSR32 receptor of about 693 amino acids.

10 More preferably, the isolated polynucleotide molecule encodes a human TSR32 receptor comprising an amino acid sequence substantially corresponding to that shown as SEQ ID NO: 2 or a functionally equivalent fragment thereof.

15 The nucleotide sequence of a polynucleotide molecule in accordance with the first aspect, may comprise a nucleotide sequence substantially corresponding to or, showing at least 75% (preferably, at least 90% or, even more preferably, at least 95%) sequence identity to that shown as SEQ ID NO: 3 or SEQ ID NO: 4 or any portion thereof encoding a functionally equivalent TSR32 receptor fragment.

20 The polynucleotide molecule may be incorporated into plasmids or expression vectors (including viral vectors), which may then be introduced into suitable host cells (e.g. bacterial, yeast, insect and mammalian host cells). Such host cells may be used to express the TSR32 receptor encoded by the isolated polynucleotide molecule.

25 Accordingly, in a second aspect, the present invention provides a host cell transformed with the polynucleotide molecule of the first aspect.

30 In a third aspect, the present invention provides a method of producing TSR32 receptors or functionally equivalent fragments thereof, comprising culturing the host cell of the second aspect under conditions enabling the expression of the polynucleotide molecule and, optionally, recovering the TSR32 receptor or fragments thereof.

35 Preferably, the host cell is mammalian or of insect origin. Where the cell is mammalian, it is presently preferred that it be a Chinese hamster ovary (CHO) cell or a human embryonic kidney (HEK) 293 cell. Where the cell is of insect origin, it is presently preferred that it be an insect Sf9 cell.

In a preferred embodiment, the TSR32 receptor or fragments thereof are expressed onto the surface of the host cells.

The polynucleotide molecules of the present invention represent a new subfamily of the secretin receptor family which may be of interest both clinically and commercially as it is expressed in many tissue types and may therefore be involved in a wide variety of systems.

5 By using the polynucleotide molecules of the present invention it is possible to obtain TSR32 receptor protein or functionally equivalent fragments thereof in a substantially pure form.

Accordingly, in a fourth aspect, the present invention provides a G-protein-coupled receptor, designated TSR32, which is characterised by the N-terminal amino acid sequence:

MTPQSLQTT (SEQ ID NO: 1),

or a functionally equivalent fragment thereof, in a substantially pure form.

Preferably, the purified TSR32 receptor has an amino acid sequence substantially corresponding to that shown as SEQ ID NO: 2.

15 In a fifth aspect, the present invention provides an antibody or antibody fragment capable of specifically binding to a TSR32 receptor according to the fourth aspect.

The antibody may be monoclonal or polyclonal, however, it is presently preferred that the antibody is a monoclonal antibody. Suitable antibody fragments include Fab, (F(ab')<sub>2</sub> and scFv.

20 In a sixth aspect, the present invention provides a non-human animal transformed with a polynucleotide molecule according to the first aspect of the present invention.

In a seventh aspect, the present invention provides a method for detecting agonist and/or antagonist compounds of the TSR32 receptor, comprising contacting a TSR32 receptor, functionally equivalent fragment thereof or a host cell transformed with and expressing the polynucleotide molecule of the first aspect, with a test compound under conditions enabling the activation of the TSR32 receptor or functionally equivalent fragment thereof, and detecting an increase or decrease in the activity of the TSR32 receptor or functionally equivalent fragment thereof.

35 An increase or decrease in activity of the receptor or functionally equivalent fragment thereof may be detected by measuring changes in CAMP production, CA<sup>2+</sup> levels or IP<sub>3</sub> turnover after activating the receptor or fragment thereof with specific agonists or antagonists.

In a further aspect, the present invention provides an oligonucleotide or polynucleotide probe comprising a nucleotide sequence of 10 or more nucleotides, the probe comprising a nucleotide sequence such that the probe specifically hybridises to the polynucleotide molecule of the first aspect under high stringency conditions (Sambrook *et al.*, *Molecular Cloning: a laboratory manual*, Second Edition, Cold Spring Harbor Laboratory Press).

Preferably the probe is labelled.

In a still further aspect, the present invention provides an antisense polynucleotide molecule comprising a nucleotide sequence capable of specifically hybridising to an mRNA molecule which encodes a TSR32 receptor so as to prevent translation of the mRNA molecule.

Such antisense polynucleotide molecules may include a ribozyme region to catalytically inactivate mRNA to which it is hybridized.

The polynucleotide molecule of the first aspect of the invention may be a dominant negative mutant which encodes a gene product causing an altered phenotype by, for example, reducing or eliminating the activity of endogenous TSR32 receptors.

The term "substantially corresponding" as used herein in relation to amino acid sequences is intended to encompass minor variations in the amino acid sequences which do not result in a decrease in the biological activity of the TSR32 receptor. These variations may include conservative amino acids substitutions. The substitutions envisaged are:-

G, A, V, I, L, M; D, E; N, Q; S, T; K, R, H; F, Y, W, H; and P,  $\alpha$ -alkalamino acids.

The term "substantially corresponding" as used herein in relation to nucleotide sequences is intended to encompass minor variations in the nucleotide sequence which due to degeneracy in the DNA code do not result in a change in the encoded protein. Further, this term is intended to encompass other minor variations in the sequence which may be required to enhance expression in a particular system but in which the variations do not result in a decrease and biological activity of the encoded protein.

The term "functionally equivalent fragment/s" as used herein is intended to refer to fragments of the TSR32 receptor that exhibit binding specificity and activity that is substantially equivalent to the full length receptor from which it/they is/are derived.

The terms "comprise", "comprises" and "comprising" as used throughout the specification are intended to refer to the inclusion of a stated step, component or feature or group of steps, components or features with or without the inclusion of a further step, component or feature or group of steps, components or features.

**Brief description of the figures:-**

Figure 1 provides the nucleotide sequence of a cDNA encoding the human TSR32 receptor and includes the predicted amino acid sequence.

Figure 2 provides a sequence alignment of the amino acid sequences of the human TSR32 receptor and the human epididymis-specific HE6 receptor (Osterhoff, C., *DNA and Cell Biology*, Vol. 16 No. 4, 1997).

**Example:-**

Degenerative oligonucleotides corresponding to conserved regions within the human Glucagon-like peptide receptor (GLP1) family were used to amplify specific DNA sequences from a variety of cDNA library DNA's. Library DNA from human hypothalamus and heart yielded fragments of the expected size. These fragments were subcloned and sequenced. One fragment, 456bp long, revealed a novel 7TM receptor sequence distantly related to the secretin receptor family. Screening a human heart cDNA library (Stratagene) using this fragment under high stringency conditions identified two positive hybridising clones, 1 and 2.9kb in size, respectively. The larger clone contains an open reading frame of 2079 nucleotides encoding a 693 amino acid long protein (designated TSR32). The nucleotide and putative amino acid sequence is provided at Figure 1.

A search of the EMBL/GenBank database revealed low but significant sequence similarities to the secretin receptor family of TM7 receptors. The sequence similarity to the above receptor sequences is only about 25% identity and also limited to the transmembrane region. However, the highest overall sequence similarity was found to four other G-protein coupled receptor subtypes, the human epididymis-specific HE6 (31% identity), the human lymphocyte antigen CD97 (33% identity), the orphan human receptor EMR1 (27% identity), the insect DHR (26% identity) and the rat latrophilin-

related protein 1 precursor (35% identity) all of which share a large extracellular domain with numerous putative O- and N-glycosylation sites. Except for DHR, in all of the receptors there is a cysteine motif preceding the first transmembrane domain. Further, in contrast to the CD97 and EMR1 receptors, TSR32 does not contain any EGF-domains or calcium binding sites in the extracellular domain.

Interestingly, at the gene level the exon/intron organisation of the TSR32-encoding cDNA, at least within the region encoding the transmembrane domain, is most similar to the gene structure of the PACAP receptor family, with fewer but identical exon/intron borders.

Northern analysis indicates a low level of expression of the receptor mRNA in a large variety of tissues including kidney, lung, cerebellum and heart. The highest level of mRNA however, was found in the thyroid gland. This expression pattern of the receptor mRNA indicates that TSR32 has important functions in metabolic regulations throughout the body via the thyroid gland.

The gene for TSR32 has been mapped to human chromosome 16q31 by *in situ* hybridisation and this localisation was confirmed by radiation hybrid analysis. An autosomal recessive disorder (Bardet Biedl Syndrome; Kwitek-Black, A.E. *et al.*, *Nature Genetics* 5: 392-396, 1993) has also been linked to this region. Features of this syndrome include obesity, retinal degeneration, hypogonadism and mental retardation. The expression of TSR32 examined by *in situ* hybridisation and Northern analysis overlaps strongly with the tissues affected in the Bardet Biedl Syndrome making TSR32 a good candidate for this locus.

It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.



Sequence listings:-

Applicant: Garvan Institute of Medical Research

Title of Invention: Novel receptor

Number of SEQ ID Nos: 4

SEQ ID NO: 1

Length: 10

Type PRT

Organism: Homo sapiens

Sequence: 1

Met	Thr	Pro	Gln	Ser	Leu	Leu	Gln	Thr	Thr
1				5					10

SEQ ID NO: 2

Length 693

Type PRT

Organism: Homo sapiens

Sequence: 2

Met	Thr	Pro	Gln	Ser	Leu	Leu	Gln	Thr	Thr	Leu	Phe	Leu	Leu	Ser	Leu
1				5					10					15	

Leu	Phe	Leu	Val	Gln	Gly	Ala	His	Gly	Arg	Gly	His	Arg	Glu	Asp	Phe
			20					25					30		

Arg	Phe	Cys	Ser	Gln	Arg	Asn	Gln	Thr	His	Arg	Ser	Ser	Leu	His	Tyr
		35					40					45			

Lys	Pro	Thr	Pro	Asp	Leu	Arg	Ile	Ser	Ile	Glu	Asn	Ser	Glu	Glu	Ala
	50					55					60				

Leu	Thr	Val	His	Ala	Pro	Phe	Pro	Ala	Ala	His	Pro	Ala	Ser	Arg	Ser
65					70					75					80

Phe	Pro	Asp	Pro	Arg	Gly	Leu	Tyr	His	Phe	Cys	Leu	Tyr	Trp	Asn	Arg
				85					90					95	

His	Ala	Gly	Arg	Leu	His	Leu	Leu	Tyr	Gly	Lys	Arg	Asp	Phe	Leu	Leu
			100					105					110		

Ser	Asp	Lys	Ala	Ser	Ser	Leu	Leu	Cys	Phe	Gln	His	Gln	Glu	Glu	Ser
		115					120					125			

Leu	Ala	Gln	Gly	Pro	Pro	Leu	Leu	Ala	Thr	Ser	Val	Thr	Ser	Trp	Trp
	130					135					140				

Ser	Pro	Gln	Asn	Ile	Ser	Leu	Pro	Ser	Ala	Ala	Ser	Phe	Thr	Phe	Ser
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

145		150		155		160
Phe His Ser Pro	Pro 165	His Thr Ala Ala	His 170	Asn Ala Ser Val	Asp 175	Met
Cys Glu Leu Lys	Arg 180	Asp Leu Gln Leu	185	Leu Ser Gln Phe	Leu 190	Lys His
Pro Gln Lys Ala	Ser 195	Arg Arg Pro	200	Ser Ala Ala Pro	205	Ser Gln Gln
Leu Gln Ser Leu	Glu 210	Ser Lys Leu Thr	215	Ser Val Arg Phe	Met 220	Gly Asp
Met Val Ser Phe	Glu 225	Glu Asp Arg Ile	230	Asn Ala Thr Val	Trp 235	Lys Leu 240
Gln Pro Thr Ala	Gly 245	Leu Gln Asp Leu	250	His Ile His Ser	Arg 255	Gln Glu
Glu Glu Gln Ser	Glu 260	Ile Met Glu Tyr	265	Ser Val Leu Leu	Pro 270	Arg Thr
Leu Phe Gln Arg	Thr 275	Lys Gly Arg Ser	280	Gly Glu Ala Glu	Lys 285	Arg Leu
Leu Leu Val Asp	Phe 290	Ser Ser Gln Ala	295	Leu Phe Gln Asp	Lys 300	Asn Ser
Ser Gln Val Leu	Gly 305	Glu Lys Val Leu	310	Gly Ile Val Val	Gln 315	Asn Thr 320
Lys Val Ala Asn	Leu 325	Thr Glu Pro Val	330	Val Leu Thr Phe	Gln 335	His Gln
Leu Gln Pro Lys	Asn 340	Val Thr Leu Gln	345	Cys Val Phe Trp	Val 350	Glu Asp
Pro Thr Leu Ser	Ser 355	Pro Gly His Trp	360	Ser Ser Ala Gly	Cys 365	Glu Thr
Val Arg Arg Glu	Thr 370	Gln Thr Ser Cys	375	Phe Cys Asn His	Leu 380	Thr Tyr
Phe Ala Val Leu	Met 385	Val Ser Ser Val	390	Glu Val Asp Ala	Val 395	His Lys 400
His Tyr Leu Ser	Leu 405	Leu Ser Tyr Val	410	Gly Cys Val Val	Ser 415	Ala Leu
Ala Cys Leu Val	Thr 420	Ile Ala Ala Tyr	425	Leu Cys Ser Arg	Val 430	Pro Leu
Pro Cys Arg Arg	Lys 435	Pro Arg Asp Tyr	440	Thr Ile Lys Val	His 445	Met Asn

Leu Leu Leu Ala Val Phe Leu Leu Asp Thr Ser Phe Leu Leu Ser Glu  
 450 455 460  
 Pro Val Ala Leu Thr Gly Ser Glu Ala Gly Cys Arg Ala Ser Ala Ile  
 465 470 475 480  
 Phe Leu His Phe Ser Leu Leu Thr Cys Leu Ser Trp Met Gly Leu Glu  
 485 490 495  
 Gly Tyr Asn Leu Tyr Arg Leu Val Val Glu Val Phe Gly Thr Tyr Val  
 500 505 510  
 Pro Gly Tyr Leu Leu Lys Leu Ser Ala Met Gly Trp Gly Phe Pro Ile  
 515 520 525  
 Phe Leu Val Thr Leu Val Ala Leu Val Asp Val Asp Asn Tyr Gly Pro  
 530 535 540  
 Ile Ile Leu Ala Val His Arg Thr Pro Glu Gly Val Ile Tyr Pro Ser  
 545 550 555 560  
 Met Cys Trp Ile Arg Asp Ser Leu Val Ser Tyr Ile Thr Asn Leu Gly  
 565 570 575  
 Leu Phe Ser Leu Val Phe Leu Phe Asn Met Ala Met Leu Ala Thr Met  
 580 585 590  
 Val Val Gln Ile Leu Arg Leu Arg Pro His Thr Gln Lys Trp Ser His  
 595 600 605  
 Val Leu Thr Leu Leu Gly Leu Ser Leu Val Leu Gly Leu Pro Trp Ala  
 610 615 620  
 Leu Ile Phe Phe Ser Phe Ala Ser Gly Thr Phe Gln Leu Val Val Leu  
 625 630 635 640  
 Tyr Leu Phe Ser Ile Ile Thr Ser Phe Gln Gly Phe Leu Ile Phe Ile  
 645 650 655  
 Trp Tyr Trp Ser Met Arg Leu Gln Ala Arg Gly Gly Pro Ser Pro Leu  
 660 665 670  
 Lys Ser Asn Ser Asp Cys Ala Arg Leu Pro Ile Ser Ser Gly Ser Thr  
 675 680 685  
 Ser Ser Ser Arg Ile  
 690

SEQ ID NO: 3  
Length 2082  
Type DNA  
Organism: Homo sapiens

## Sequence: 3

atgactcccc	agtcgctgct	gcagacgaca	ctgttcctgc	tgagtctgct	cttcctgggtc	60
caaggtgccc	acggcagggg	ccacagggaa	gacttttcgt	tctgcagcca	gcggaaccag	120
acacacagga	gcagcctcca	ctacaaaccc	acaccagacc	tgcgcattct	catcgagaac	180
tccgaagagg	ccctcacagt	ccatgcccct	ttccctgcag	cccaccctgc	ttcccgatcc	240
ttccctgacc	ccaggggccc	ctaccacttc	tgcctctact	ggaaccgaca	tgctgggaga	300
ttacatcttc	tctatggcaa	gcgtgacttc	ttgctgagtg	acaaagcctc	tagcctcctc	360
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acctcctggg	ggagccctca	gaacatcagc	ctgcccagtg	ccgccagctt	caccttctcc	480
ttccacagtc	ctccccacac	ggccgctcac	aatgcctcgg	tggacatgtg	cgagctcaaa	540
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tcggctgccc	ccgccagcca	gcagttgcag	agcctggagt	cgaaactgac	ctctgtgaga	660
ttcatggggg	acatggtgtc	cttcgaggag	gaccggatca	acgccacggg	atggaagctc	720
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ccccacaccc	aaaagtgggt	acatgtgctg	acactgctgg	gcctcagcct	ggctccttggc	1860
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taccttttca	gcacatcac	ctccttccaa	ggcttctcca	tcttcatctg	gtactgggtcc	1980
atgcggctgc	aggcccgggg	tggccccctc	cctctgaaga	gcaactcaga	ctgcgccagg	2040
ctccccatca	gctcgggcag	cacctcgtcc	agccgcattc	ag		2082

SEQ ID NO: 4  
Length 2834  
Type DNA  
Organism: Homo sapiens

## Sequence: 4

gaattccggc	agcagggtct	cgctctgtca	cacaggctgg	agtgcagtgg	tgtgatcttg	60
gctcatcgta	acctccacct	cccgggttca	agtgattctc	atgcctcagc	ctcccagagta	120
gctgggatta	caggtgggtga	cttccaagag	tgactccgtc	ggaggaaaat	gactccccag	180
tcgctgctgc	agacgacact	gttccctgctg	agtctgctct	tcctgggtcca	aggtgcccac	240
ggcagggggc	acagggaaga	ctttcgcttc	tgcagccagc	ggaaccagac	acacaggagc	300

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ctcacagtcc	atgccccttt	cctgcagccc	caccctgctt	cccgatcctt	ccctgacccc	420
aggggcctct	accacttctg	cctctactgg	aaccgacatg	ctgggagatt	acatcttctc	480
tatggcaagc	gtgacttctt	gctgagtgc	aaagcctcta	gcctcctctg	cttccagcac	540
caggaggaga	gcctggctca	gggccccccg	ctgttagcca	cttctgtcac	ctcctgggtg	600
agccctcaga	acatcagcct	gccagtgccc	gccagcttca	ccttctcctt	ccacagtcc	660
ccccacacgg	ccgctcacia	tgcctcgggtg	gacatgtgcg	agctcaaaag	ggacctccag	720
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ctcacggagc	ccgtggtgct	cactttccag	caccagctac	agccgaagaa	tgtgactctg	1200
caatgtgtgt	tctgggttga	agacccccca	ttgagcagcc	cggggcattg	gagcagtgtc	1260
gggtgtgaga	ccgtcaggag	agaaacccaa	acatcctgct	tctgcaacca	cttgacctac	1320
tttgagtgct	tgatggtctc	ctcgggtggag	gtggacgccc	tgacaagca	ctacctgagc	1380
ctcctctcct	acgtgggctg	tgctgtctct	gccctggcct	gccttgtcac	cattgccgcc	1440
tacctctgct	ccagggtgcc	cctgccgtgc	aggaggaaac	ctcgggacta	caccatcaag	1500
gtgcacatga	acctgctgct	ggccgtcttc	ctgctggaca	cgagcttcct	gctcagcgag	1560
ccggtggccc	tgacaggctc	tgaggctggc	tgccgagcca	gtgccatctt	cctgcacttc	1620
tccttgcctc	cctgcctttc	ctggatgggc	ctcagggggt	acaacctcta	ccgactcgtg	1680
gtggagggtc	ttggcaccta	tgtccctggc	tacctactca	agctgagcgc	catgggctgg	1740
ggcttcccca	tctttctggt	gacgctgggtg	gccctgggtg	atgtggacaa	ctatggcccc	1800
atcatcttgg	tgctgcatag	gactccagag	ggcgtcatct	acccttccat	gtgctggate	1860
cgggactccc	tggctagcta	catcaccaac	ctgggcctct	tcagcctggt	gtttctgttc	1920
aacatggcca	tgctagccac	catggtgggtg	cagatccctgc	ggctgcgccc	ccacacccaa	1980
aagtgggtcac	atgtgctgac	actgctgggc	ctcagcctgg	tccttggcct	gccctggggc	2040
ttgatcttct	tctcctttgc	ttctggcacc	ttccagcttg	tcgtcctcta	ccttttcagc	2100
atcatcacct	ccttccaagg	cttctctatc	ttcatctggt	actggtccat	gcggctgcag	2160
gccgggggtg	gcccctcccc	tctgaagagc	aactcagact	gcgccaggct	ccccatcagc	2220
tcgggcagca	cctcgtccag	ccgcatctag	gcctccagcc	cacctgccca	tgtgatgaag	2280
cagagatgcy	gcctcgtcgc	acactgcctg	tgccccccga	gccaggccca	gccccaggcc	2340
agtacagccg	agacttttga	aagcccaacg	accatggaga	gatgggcccgt	tgccatgggtg	2400
gacggactcc	cggggctggg	gcttttgaat	tgcccttggg	gactactcgg	ctctcactca	2460
gctcccacgg	gactcagaag	tgcgccgcca	tgctgcctag	ggtactgtcc	ccacatctgt	2520
cccaacccag	ctggaggcct	ggtctctcct	tacaacccct	gggcccagcc	tcattgctgg	2580
gggccaggcc	ttggatcttg	aggggtctggc	acatccttaa	tcctgtgccc	ctgcctggga	2640
cagaaatgtg	gctccagttg	ctctgtctct	cgtgggtcacc	ctgagggcac	tctgcatacct	2700
ctgtcatttt	aacctcaggt	ggcaccacag	gcgaatgggg	cccagggcag	accttcaggg	2760
ccagagccct	ggcgaggag	aggccctttg	ccaggagcac	agcagcagct	cgcctacctc	2820
tgagcccga	attc					2834

**Claims:**

1. An isolated polynucleotide molecule encoding a G-protein-coupled receptor which is characterised by the N-terminal amino acid sequence:

5 MTPQSLLQTT (SEQ ID NO: 1),

or a functionally equivalent fragment of said receptor.

2. A polynucleotide molecule according to claim 1, wherein said polynucleotide molecule encodes a G-protein-coupled receptor of human  
10 origin of about 693 amino acids in length.

3. A polynucleotide molecule according to claim 2, wherein the polynucleotide molecule encodes a G-protein-coupled receptor comprising an amino acid sequence substantially corresponding to that shown as SEQ ID  
15 NO: 2.

4. An isolated polynucleotide molecule encoding a G-protein-coupled receptor, wherein the polynucleotide molecule comprises a nucleotide sequence showing at least 75% sequence identity to that shown as SEQ ID  
20 NO: 3 or SEQ ID NO: 4 or any portion thereof encoding a functionally equivalent receptor fragment.

5. A polynucleotide molecule according to claim 4, wherein the polynucleotide molecule comprises a nucleotide sequence showing at least  
25 90% sequence identity to that shown as SEQ ID NO: 3 or SEQ ID NO: 4 or any portion thereof encoding a functionally equivalent receptor fragment.

6. A polynucleotide molecule according to claim 5, wherein the polynucleotide molecule comprises a nucleotide sequence showing at least  
30 95% sequence identity to that shown as SEQ ID NO: 3 or SEQ ID NO: 4 or any portion thereof encoding a functionally equivalent receptor fragment.

7. A plasmid or expression vector including a polynucleotide molecule according to any one of the preceding claims.  
35

8. A host cell transformed with a polynucleotide molecule according to any one of claims 1 to 6.

9. A host cell according to claim 8, wherein the cell is a mammalian or insect cell.

10. A host cell according to claim 9, wherein the cell is a Chinese hamster ovary (CHO) cell, human embryonic kidney (HEK) 293 cell or an insect Sf9 cell.

11. A host cell according to any one of claims 8 to 10 wherein the cell expresses the G-protein-coupled receptor or functionally equivalent fragment thereof onto the cell's surface.

12. A G-protein-coupled receptor which is characterised by the N-terminal amino acid sequence:

MTPQSLLQTT (SEQ ID NO: 1),  
or a functionally equivalent fragment of said receptor, in a substantially pure form.

13. A receptor according to claim 12, wherein said receptor is a human receptor of about 693 amino acids.

14. A receptor according to claim 13, wherein the receptor has an amino acid sequence substantially corresponding to that shown as SEQ ID NO: 2.

15. An antibody or fragment thereof which specifically binds to a G-protein-coupled receptor according to any one of claims 12 to 14.

16. A non-human animal transformed with a polynucleotide molecule according to any one of claims 1 to 6.

17. A method for detecting agonist or antagonist agents of a G-protein-coupled receptor comprising, contacting a G-protein-coupled receptor according to any one of claims 12 to 14 or a host cell transformed with and expressing a DNA molecule according to any one of claims 1 to 6, with a test

agent under conditions enabling the activation of the receptor, and detecting an increase or decrease in the receptor activity.

- 5 18. An oligonucleotide or polynucleotide probe comprising a nucleotide sequence of 10 or more nucleotides, the probe comprising a nucleotide sequence such that the probe specifically hybridises to the polynucleotide molecule of any one of claims 1 to 6 under high stringency conditions.
- 10 19. An antisense polynucleotide molecule comprising a nucleotide sequence capable of specifically hybridising to an mRNA molecule which encodes a G-protein-coupled receptor encoded by the polynucleotide molecule of any one of claims 1 to 6, so as to prevent translation of the mRNA molecule.
- 15 20. A method of producing G-protein-coupled receptors or functionally equivalent fragments thereof according to any one of claims 12 to 14, comprising culturing a host cell according to any one of claims 8 to 11 under conditions enabling the expression of the polynucleotide molecule and optionally recovering the receptors or functionally equivalent fragments
- 20 thereof.



FIGURE 1

1/5

70  
GAATTCCGGCAGCAGGGTCTCGCTCTGTACACAGGCTGGAGTGCAGTGGTGTGATCTTGGCTCATCGTA

140  
ACCTCCACCTCCCGGGTTCAAGTGATTCTCATGCCTCAGCCTCCCGAGTAGCTGGGATTACAGGTGGTGA

210  
CTTCCAAGAGTGACTCCGTCGGAGGAAAATGACTCCCCAGTCGCTGCTGCAGACGACACTGTTCTGCTG  
M T P Q S L L Q T T L F L L>

280  
AGTCTGCTCTTCTGGTCCAAGGTGCCCACGGCAGGGGCCACAGGGAAGACTTTCGCTTCTGCAGCCAGC  
S L L F L V Q G A H G R G H R E D F R F C S Q>

350  
GGAACCAGACACACAGGAGCAGCCTCCACTACAAACCCACACCAGACCTGCGCATCTCCATCGAGAACTC  
R N Q T H R S S L H Y K P T P D L R I S I E N S>

420  
CGAAGAGGCCCTCACAGTCCATGCCCCCTTCCCTGCAGCCCACCCTGCTTCCCGATCCTTCCCTGACCCC  
E E A L T V H A P F P A A H P A S R S F P D P>

490  
AGGGGCCTCTACCACTTCTGCCTCTACTGGAACCGACATGCTGGGAGATTACATCTTCTCTATGCCAAGC  
R G L Y H F C L Y W N R H A G R L H L L Y G K>

560  
GTGACTTCTTGCTGAGTGACAAAGCCTCTAGCCTCCTCTGCTTCCAGCACCAGGAGGAGAGCCTGGCTCA  
R D F L L S D K A S S L L C F Q H Q E E S L A Q>

630  
GGGCCCCCGCTGTAGCCACTTCTGTACCTCCTGGTGGAGCCCTCAGAACATCAGCCTGCCCAGTGCC  
G P P L L A T S V T S W W S P Q N I S L P S A>

700  
GCCAGCTTACCTTCTCCTTCCACAGTCCTCCCCACACGGCCGCTCACAATGCCTCGGTGGACATGTGCG  
A S F T F S F H S P P H T A A H N A S V D M C>

770  
AGCTCAAAAGGGACCTCCAGCTGCTCAGCCAGTTCTGAAGCATCCCCAGAAGGCCTCAAGGAGGGCCCTC  
E L K R D L Q L L S Q F L K H P Q K A S R R P S>

840  
GGCTGCCCCCGCCAGCCAGCAGTTGCAGAGCCTGGAGTCGAAACTGACCTCTGTGAGATTATGGGGGAC  
A A P A S Q Q L Q S L E S K L T S V R F M G D>

910

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2/5

ATGGTGTCTTTCGAGGAGGACCGGATCAACGCCACGGTATGGAAGCTCCAGCCCACAGCCGGCCTCCAGG  
M V S F E E D R I N A T V W K L Q P T A G L Q>

980

ACCTGCACATCCACTCCCGGCAGGAGGAGGAGCAGAGCGAGATCATGGAGTACTCGGTGCTGCTGCCTCG  
D L H I H S R Q E E E Q S E I M E Y S V L L P R>

1050

AACACTCTTCCAGAGGACGAAAGGCCGAGCGGGAGGCTGAGAAGAGACTCCTCCTGGTGGACTTCAGC  
T L F Q R T K G R S G E A E K R L L L V D F S>

1120

AGCCAAGCCCTGTTCCAGGACAAGAATTCCAGCCAAGTCCTGGGTGAGAAGGTCTTGGGGATTGTGGTAC  
S Q A L F Q D K N S S Q V L G E K V L G I V V>

1190

AGAACACCAAAGTAGCCAACCTCACGGAGCCCGTGGTGCTCACTTTCCAGCACCAGCTACAGCCGAAGAA  
Q N T K V A N L T E P V V L T F Q H Q L Q P K N>

1260

TGTGACTCTGCAATGTGTGTTCTGGGTTGAAGACCCACATTGAGCAGCCCGGGGCATTGGAGCACTGCT  
V T L Q C V F W V E D P T L S S P G H W S S A>

1330

GGGTGTGAGACCGTCAGGAGAGAAACCCAAACATCCTGCTTCTGCAACCACTTGACCTACTTTGCAGTGC  
G C E T V R R E T Q T S C F C N H L T Y F A V>

1400

TGATGGTCTCCTCGGTGGAGGTGGACGCCGTGCACAAGCACTACCTGAGCCTCCTCTCCTACGTGGGCTG  
L M / S S V E V D A V H K H Y L S L L S Y V G C>

1470

TGTCGTCTCTGCCCTGGCCTGCCTTGTCACCATTGCCGCTACCTCTGCTCCAGGGTGCCCCCTGCCGTGC  
V V S A L A C L V T I A A Y L C S R V P L P C>

1540

AGGAGGAAACCTCGGGACTACACCATCAAGGTGCACATGAACCTGCTGCTGGCCGTCTTCTGCTGGACA  
R R K P R D Y T I K V H M N L L L A V F L L D>

1610

CGAGCTTCTGCTCAGCGAGCCGGTGGCCCTGACAGGCTCTGAGGCTGGCTGCCGAGCCAGTGCCATCTT  
T S F L L S E P V A L T G S E A G C R A S A .I F>

1680

CCTGCACTTCTCCCTGCTCACCTGCCTTTCTGGATGGGCCTCGAGGGGTACAACCTCTACCGACTCGTG  
L H F S L L T C L S W M G L E G Y N L Y R L V>

1750

GTGGAGGTCTTTGGCACCTATGTCCCTGGCTACCTACTCAAGCTGAGCGCCATGGGCTGGGGCTTCCCCA  
V E V F G T Y V P G Y L L K L S A M G W G F P>

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3/5

1820  
\* \* \* \* \*  
TCTTTCTGGTGACGCTGGTGGCCCTGGTGGATGTGGACAACTATGGCCCCATCATCTTGGCTGTGCATAG  
I F L V T L V A L V D V D N Y G P I I L A V H R>

1890  
\* \* \* \* \*  
GACTCCAGAGGGCGTCATCTACCCTTCCATGTGCTGGATCCGGGACTCCCTGGTCAGCTACATCACCAAC  
T P E G V I Y P S M C W I R D S L V S Y I T N>

1960  
\* \* \* \* \*  
CTGGGCCTCTTCAGCCTGGTGTCTTCTGTTCAACATGGCCATGCTAGCCACCATGGTGGTGCAGATCCTGC  
L G L F S L V F L F N M A M L A T M V V Q I L>

2030  
\* \* \* \* \*  
GGCTGCGCCCCACACCCAAAAGTGGTCACATGTGCTGACACTGCTGGGCCTCAGCCTGGTCTTGGCCT  
R L R P H T Q K W S H V L T L L G L S L V L G L>

2100  
\* \* \* \* \*  
GCCCTGGGCCTTGATCTTCTTCTCCTTTGCTTCTGGCACCTTCCAGCTTGTCTCCTCTACCTTTTCAGC  
P W A L I F F S F A S G T F Q L V V L Y L F S>

2170  
\* \* \* \* \*  
ATCATCACCTCCTTCCAAGGCTTCCTCATCTTCATCTGGTACTGGTCCATGCGGCTGCAGGCCCCGGGTG  
I I T S F Q G F L I F I W Y W S M R L Q A R G>

2240  
\* \* \* \* \*  
GCCCTCCCCTCTGAAGAGCAACTCAGACTGCGCCAGGCTCCCCATCAGCTCGGGCAGCACCTCGTCCAG  
G P S P L K S N S D C A R L P I S S G S T S S S>

2310  
\* \* \* \* \*  
CCGCATCTAGGCCTCCAGCCCACCTGCCCATGTGATGAAGCAGAGATGCGGCCTCGTCGCACACTGCCTG  
R I>

2380  
\* \* \* \* \*  
TGGCCCCCGAGCCAGGCCAGCCCCAGGCCAGTCAGCCGCAGACTTTGGAAAGCCCAACGACCATGGAGA

2450  
\* \* \* \* \*  
GATGGGCCGTTGCCATGGTGGACGGACTCCCGGGGCTGGGGCTTTGAATTGGCCTTGGGGACTACTCGG

2520  
\* \* \* \* \*  
CTCTCACTCAGCTCCCACGGGACTCAGAAGTGCGCCGCCATGCTGCCTAGGGTACTGTCCCCACATCTGT

2590  
\* \* \* \* \*  
CCCAACCCAGCTGGAGGCCTGGTCTCTCCTTACAACCCCTGGGCCCAGCCTCATTGCTGGGGGCCAGGCC

2660  
\* \* \* \* \*  
TTGGATCTTGAGGGTCTGGCACATCCTTAATCCTGTGCCCTGCCTGGGACAGAAATGTGGCTCCAGTTG

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4/5

CTCTGTCTCTCGTGGTCACCCCTGAGGGCACTCTGCATCCTCTGTCATTTTAACCTCAGGTGGCACCCAGG  
GCGAATGGGGCCCAGGGCAGACCTTCAGGGCCAGAGCCCTGGCGGAGGAGAGGCCCTTTGCCAGGAGCAC  
AGCAGCAGCTCGCCTACCTCTGAGCCCGGAATTC

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FIGURE 2

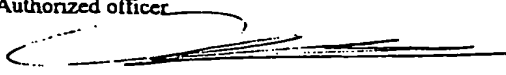
5/5

hU32p 1 MFSVRQCGHVGRTEEVLLTFKIFLVIIICLHVVLVTSLEEDTDNSSLSPPAKLSVVSFA PSSNEVET  
 HE6p 1  
 hU32p 1 SLNDVTLSSLPSNETEKTITIVKTFNAGVKPORNICNLSSICNDSAFFRGEIMFOYDKESTVPONOH  
 HE6p 70  
 hU32p 1 ITNGITGLVLSLSEELKRSELNKTLQTLSETYFIMCATAEAOSTLNCFTIKLNTMNACAAIAALERVK  
 HE6p 139  
 hU32p 1 MTPQSLQTLFLLSLFLVOGAHGRGHREDFRFCQRNTHRSSLHYKPTPOLRIS  
 HE6p 208 IRPMEHCSCSVRIPCPSISPEELGKLOCODLPVCLADHPHGPFFSSOSIPVVPRAIVLSOVPAKATSF  
 hU32p 58 IENSEALTVRAFPFAAHPRSRSFPDPRGLYHFCLYWNRHAGRLHLLYGKRDFLSDKASSLLCFOHOE  
 HE6p 277 AEPDPDYSPVTINVPSPIGEIOPLSBOPASAP IASSPAIDMPOSETISSPMOTHVSGTPPVKASFSSP  
 hU32p 127 ESLAOGPPLLATSVTSWSPQNISLPASAFSFSFHSPPHTAAHNASVDMCELRKRDLOLISOFLKHPOK  
 HE6p 346 TVSA PANVNNTTSAPVOTDIVNTSSISDLENOVLOMEKALSLGSEPNLAGEMINOVSRLLHSPDMLA  
 hU32p 196 ASARPSAAPASOQLOSLESKLTSVRFMGDMVSFEEDRIINATVWKLOPTAGLODLHHSROEEEOSEIME  
 HE6p 415 PLAORLKVVDIGLQINFSNITISLTSPLALAVIRVNASFNITTFVAODPANLOVSLTOAPEINSI  
 hU32p 265 YSVLPLRTLFORTKGRSGEAEKRLLLVDFFSSQALFODKNSSOVLEGEKVLGIVVQNTKVANLTPVVL  
 HE6p 484 GTITLPSLLMNNLPAHDMELASRVOFNFEETPALFOODPSLENLSLISVYISSSVANLTVRNLTRANVIT  
 hU32p 333 FQHLOLPKN-VTLQCVFWVEDPTLSSPGHWSAGCE-TVRRRETQTSQFCNHLTYFAVLMSVSEVDAVH  
 HE6p 553 LKHINPSODELTVRCYEW-DLGRNGRGCGWSDNGCSVKDRRLNETIICSHLTSIEGVLLDLSRTSVLPA  
 hU32p 400 KH-YLSLSYVGVVSAALACLVTIAAYLCRAVPLPCRAKPRDYTIKVMNLVLAVFLDTSFLSEPA  
 HE6p 621 OMMALLTITYIGGGLSSIFLSVTLVIAAFLCSRAVPLPCRAKPRDYTIKVMNLVLAVFLDTSFLSEPA  
 hU32p 468 LTGSEAGCRASAIIFLHFSLLTCLSMGLEGYNLVRLVVEVFGTYVPGYLKLISAMGWGFPIFLVTLVAL  
 HE6p 689 .....GLCISVAVELHYFLLVSTWMGLEAFHMYLALVKVFNITYIRKYLKFCIVGWGVBAVVVITIL  
 hU32p 537 VDV DNYGPIILAVHRTPEGV IYPSMCMWRDLSVSYITNGLSLVFLFNMAMLATMVVQILRLRPHITOK  
 HE6p 753 ISP DNYGLGSYG...KFPNGSPDDFCWJNNNAVIFYITVVGVYECVIELLVSVFIVVLVQLCBIKKKKOL  
 hU32p 606 WSHVTL-LGLSLVLGLPWALLIFFSFAAGTQOLV...LYLFSITSFQGFLLTFIMYMSMLQARGGP  
 HE6p 819 GAORKTTSIODLRSAIGLTFLLGITWGFATFAWGPVNVITFMYLEAIFNTLOGFFLEIFYCVAKENVBKOW  
 hU32p 670 SPLKSNSDCARLPISGSGSTSSRI  
 HE6p 888 RRYLCCGKLRLAENSOWSKTATNGLKOTVNOGVSSSSNSLOSSSNSNSTLLLVNDCSVHASGNGNA  
 HE6p 957 STERNGVSVSONGDVCLHDFTGKOHMFNEKEDESCNGKGRMALRRTSKRGLHFIEO

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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/AU 98/00805

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>												
Int Cl <sup>6</sup> : C07K 7/06, 14/705, 16/28, C12N 15/12, 5/10, C12P 21/02, A01K 67/027, G01N 33/68, C07H 21/04												
According to International Patent Classification (IPC) or to both national classification and IPC												
<b>B. FIELDS SEARCHED</b>												
Minimum documentation searched (classification system followed by classification symbols) See below												
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched												
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) STN, File Reg, "MTPQSLQTT/SQSP" Gen Bank, Swiss Prot., EMBL, PIR: SEQ ID. No 1, SEQ ID. No 2												
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>												
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.										
X	Biochemical and Biophysical Research Communications vol. 198 No. 1 (1994) Pages 328-334; MacNeil, Douglas J., et al. "Cloning and Expression of a Human Glucagon Receptor" Abstract, figure 1	18,19										
X	DNA and Cell Biology vol. 16, No. 4 (1997) pages 379-389. Osterhoff, C et al "Cloning of a Human Epididymus-Specific mRNA, He6, Encoding an Novel Member of the Seven Transmembrane-Domain Receptor Superfamily" Abstract, figure 4, page 381 column 1	18,19										
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input type="checkbox"/> See patent family annex												
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"E" earlier application or patent but published on or after the international filing date</td> <td>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention											
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone											
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art											
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family											
"P" document published prior to the international filing date but later than the priority date claimed												
Date of the actual completion of the international search 13 November 1998		Date of mailing of the international search report 17 NOV 1998										
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No.: (02) 6285 3929		Authorized officer  <b>CHRISTINE BREMERS</b> Telephone No.: (02) 6283 2313										

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU 98/00805

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Gene, vol 140 (1994) pages 203-209, Lok. S et al "The Human Glucagon receptor encoding gene: structure, cDNA sequence and chromosomal localization" whole document, especially page 203 column 2, page 204 column 2 part (c), figure 1.	18,19
P,X	Biochimica et Biophysica Acta 1395 (1998) pages 301-308, Mayer, H et al. "Isolation, molecular characterization, and tissue-specific expression of a novel putative G protein-coupled receptor" Abstract; figure 2.; page 307 column 1, last paragraph.	18,19